

Claims

1. The use of an isolated proton-sensing GPCR polypeptide in the development of a medicament for disease and medical conditions in which proton homeostasis is imbalanced.
2. The use of an isolated proton-sensing GPCR polypeptide in the development of a medicament for disease and medical conditions in which proton homeostasis is imbalanced; said polypeptide is selected from one of the groups consisting of:
 - (a) an isolated polypeptide encoded by a polynucleotide comprising the polynucleotide sequence of human OGR1 (accession number: NM_003485.1), rat OGR1 (accession number: XM_234483), mouse OGR1 (accession number: NM_175493), bovine OGR1 (accession number: NM_174329), preferably human OGR1 (accession number: NM_003485.1), human GPR4 (accession number: NM_005282), mouse GPR4 (accession number: NM_175668), human TDAG8 (accession number: NM_003608) and mouse TDAG8 (accession number: NM_008152);
 - (b) an isolated proton sensing GPCR polypeptide comprising a polypeptide sequence having at least 20% to the polypeptide sequence of SEQ ID NO: 1;
 - (c) an isolated proton sensing GPCR polypeptide comprising a polypeptide sequence having at least 20% to the polypeptide sequence of SEQ ID NO: 3;
 - (d) an isolated proton sensing GPCR polypeptide comprising a polypeptide sequence having at least 20% identity to the polypeptide sequence of SEQ ID NO: 4;
 - (e) an isolated polypeptide comprising the polypeptide sequence of SEQ ID NO: 1, SEQ ID NO: 3 or SEQ ID NO: 4;
 - (f) an isolated proton sensing GPCR polypeptide having at least 20% identity to the polypeptide sequence of SEQ ID NO: 1;
 - (g) an isolated proton sensing GPCR polypeptide having at least 20% identity to the polypeptide sequence of SEQ ID NO: 3;
 - (h) an isolated proton sensing GPCR polypeptide having at least 20% identity to the polypeptide sequence of SEQ ID NO: 4;
 - (i) the polypeptide sequences of SEQ ID NO: 1, SEQ ID NO: 3, or SEQ ID NO: 4; and
 - (l) polypeptides in (a) to (i) which show a pH dependent Inositol phosphate formation in CCL39 hamster fibroblast cells or a pH dependent signal in the cAMP luciferase reporter assay in CHOK1 CRE-luc cells or CCL39 CRE-luc cells.

3. The use of the isolated polypeptide as claimed in claim 1 or 2, said polypeptide comprising the polypeptide sequence of SEQ ID NO: 1, SEQ ID NO: 3 or SEQ ID NO: 4.
4. The use of the isolated polypeptide as claimed in claim 1 or 2, said polypeptide consisting of the polypeptide sequence of SEQ ID NO: 1, SEQ ID NO: 3 or SEQ ID NO: 4.
5. The use of an isolated polynucleotide in the development of a medicament for the prevention and treatment of diseases and medical conditions in which proton homeostasis is imbalanced; said polynucleotide is selected from one of the groups consisting of:
 - (a) an isolated polynucleotide comprising the polynucleotide sequence of human OGR1 (accession number: NM_003485.1), rat OGR1 (accession number: XM_234483), mouse OGR1 (accession number: NM_175493), bovine OGR1 (accession number: NM_174329), preferably human OGR1 (accession number: NM_003485.1), human GPR4 (accession number: NM_005282), mouse GPR4 (accession number: NM_175668), human TDAG8 (accession number: NM_003608) and mouse TDAG8 (accession number: NM_008152);
 - (b) an isolated polynucleotide encoding a proton sensing GPCR polypeptide sequence having at least 20% identity to the polypeptide sequence of SEQ ID NO: 1;
 - (c) an isolated polynucleotide encoding a proton sensing GPRC polypeptide sequence having at least 20% identity to the polypeptide sequence of SEQ ID NO: 3;
 - (d) an isolated polynucleotide encoding a proton sensing GPRC polypeptide sequence having at least 20% identity to the polypeptide sequence of SEQ ID NO: 4;
 - (f) an isolated polynucleotide comprising the polynucleotide sequence of human OGR1 (accession number: NM_003485.1), rat OGR1 (accession number: XM_234483), mouse OGR1 (accession number: NM_175493), bovine OGR1 (accession number: NM_174329), preferably human OGR1 (accession number: NM_003485.1), human GPR4 (accession number: NM_005282), mouse GPR4 (accession number: NM_175668), human TDAG8 (accession number: NM_003608) and mouse TDAG8 (accession number: NM_008152);
 - (g) the polynucleotide sequences of human OGR1 (accession number: NM_003485.1), rat OGR1 (accession number: XM_234483), mouse OGR1 (accession number: NM_175493), bovine OGR1 (accession number: NM_174329), preferably human OGR1 (accession number: NM_003485.1), human GPR4 (accession number: NM_005282), mouse GPR4 (accession number: NM_175668), human TDAG8 (accession number: NM_003608) and mouse TDAG8 (accession number: NM_008152); and

(h) polynucleotides in (a) to (g) which encode for a polypeptide that show a pH dependent Inositol phosphate formation in CCL39 hamster fibroblast cells or a pH dependent signal in the cAMP luciferase reporter assay in CHOK1 CRE-luc cells or CCL39 CRE-luc cells.

6. The use of an antibody, which specifically binds to a polypeptide of any one of the claims 1 to 4, for the manufacture of a medicament for the prevention and/or treatment of diseases and medical conditions in which proton homeostasis is imbalanced;

a pharmaceutical composition comprising an antibody for the prevention and/or treatment of diseases and medical conditions in which proton homeostasis is imbalanced, said antibody specifically binds to a polypeptide of any one of the claims 1 to 4; or

a method of prevention and/or treatment of diseases and medical conditions in which proton homeostasis is imbalanced comprising administering to a subject in need of such prevention and/or treatment an effective amount of an antibody, said antibody specifically binds to a polypeptide of any one of the claims 1 to 4.

7. A method for screening to identify compounds that antagonize the proton-sensing activity of the polypeptides according to any one of claims 1 to 4.

8. A method for screening to identify compounds that agonize the proton-sensing activity of the polypeptides according to any one of claims 1 to 4.

9. A method for screening to identify compounds that stimulate or inhibit the function or expression level of the polypeptides of claims 1 to 4 comprising a method selected from the group consisting of:

(a) measuring or, detecting, quantitatively or qualitatively, the binding of a candidate compound to the polypeptide (or to the cells or membranes expressing the polypeptide) or a fusion protein thereof by means of a label directly or indirectly associated with the candidate compound;

(b) measuring the competition of binding of a candidate compound to the polypeptide (or to the cells or membranes expressing the polypeptide) or a fusion protein thereof in the presence of a labelled competitor;

(c) testing whether the candidate compound results in a signal generated by activation or inhibition of the polypeptide, using detection systems appropriate to the cells or cell membranes expressing the polypeptide; or

(d) detecting the effect of a candidate compound on the production of mRNA encoding said polypeptide or said polypeptide in cells, using for instance, an ELISA assay.

10. A method of prevention and/or treatment of diseases and medical conditions in which proton homeostasis is imbalanced comprising administering to a subject in need of such prevention and/or treatment an effective amount of an antagonist obtainable from the method of claim 7.

11. A method of prevention and/or treatment of diseases and medical conditions in which proton homeostasis is imbalanced comprising administering to a subject in need of such prevention and/or treatment an effective amount of an agonist obtainable from the method of claim 8.

12. A pharmaceutical composition for the prevention and/or treatment of diseases and medical conditions in which proton homeostasis is imbalanced comprising an antagonist obtainable from the method of claim 7.

13. A pharmaceutical composition for the prevention and/or treatment of diseases and medical conditions in which proton homeostasis is imbalanced comprising an agonist obtainable from the method of claim 8.

14. A diagnostic kit comprising an antibody against a polypeptide according to any one of claims 1 to 4.

15. A diagnostic kit comprising a pharmaceutical preparation for the prevention and/or treatment of diseases and medical conditions in which proton homeostasis is imbalanced, said pharmaceutical preparation comprising an antibody against a polypeptide according to any one of claims 1 to 4.